

FIG. 1A Structural motifs in GRBP2

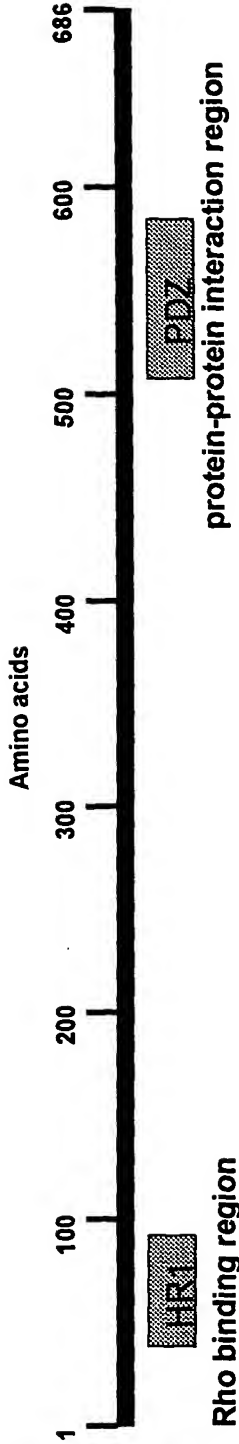


Fig. 1B HR1 domains

| | | | | | | | |
|------------|---|----|----|----|----|----|----|
| consensus | 1 | 10 | 20 | 30 | 40 | 50 | 60 |
| GRBP2 | 1 | 10 | 20 | 30 | 40 | 50 | 60 |
| gi 7503594 | 1 | 10 | 20 | 30 | 40 | 50 | 60 |
| gi 6093970 | 1 | 10 | 20 | 30 | 40 | 50 | 60 |
| gi 543444 | 1 | 10 | 20 | 30 | 40 | 50 | 60 |
| gi 6319363 | 1 | 10 | 20 | 30 | 40 | 50 | 60 |
| gi 6225859 | 1 | 10 | 20 | 30 | 40 | 50 | 60 |
| gi 1085218 | 1 | 10 | 20 | 30 | 40 | 50 | 60 |
| gi 1175418 | 1 | 10 | 20 | 30 | 40 | 50 | 60 |

| | | | | | | | | |
|------------|----|----|----|----|----|-----|-----|-----|
| consensus | 53 | 60 | 70 | 80 | 90 | 100 | 110 | 120 |
| GRBP2 | 53 | 60 | 70 | 80 | 90 | 100 | 110 | 120 |
| gi 7503594 | 53 | 60 | 70 | 80 | 90 | 100 | 110 | 120 |
| gi 6093970 | 53 | 60 | 70 | 80 | 90 | 100 | 110 | 120 |
| gi 543444 | 53 | 60 | 70 | 80 | 90 | 100 | 110 | 120 |
| gi 6319363 | 53 | 60 | 70 | 80 | 90 | 100 | 110 | 120 |
| gi 6225859 | 53 | 60 | 70 | 80 | 90 | 100 | 110 | 120 |
| gi 1085218 | 53 | 60 | 70 | 80 | 90 | 100 | 110 | 120 |
| gi 1175418 | 53 | 60 | 70 | 80 | 90 | 100 | 110 | 120 |

Fig. 1C PDZ domains

| | | | | | | | |
|-------------|-----|---|--------------------|----------------------|---------------------|--------|----|
| | | 10 | 20 | 30 | 40 | 50 | 60 |
| | |*.....*.....*.....*.....*..... | | | | | |
| consensus | 1 | EPRIVELEKGG | ---GGLGFSLVGGKDSgd | ----- | GGVVSSVVPSPAAKAG | ---44 | |
| GRBP2 | 513 | PPRSIRFTAE | ---GDLGFTLRGNA | ----- | PVQVHFDPYCSASVAG | ---551 | |
| gi 13096475 | 70 | PRLAALRRGTag | vtGVGLEITYDGSg | ----- | KDVVLTTPAGGPAEKAG | ---116 | |
| gi 7512038 | 405 | EPFISFQKE | ---GSVGIRLTGgn | ----- | eAGIFVTAVQPGSPASLQg | ---444 | |
| gi 6671754 | 484 | EPRTVEIIRLS | ---DALGISIAGGKSPlg | ----- | dIPFIAMIQANGVAARTQk | ---531 | |
| gi 7662086 | 44 | VQRCVLIQKQ | ---HGFGFTVSGD | ----- | RIVLVQSVRPPGGAAMKAG | ---82 | |
| gi 131530 | 507 | YLVLRITPDe | ---dGKGFNLKGGVDq | ----- | kMPLVSRINPESPADTCIp | ---551 | |
| gi 6093970 | 497 | LVGPHMTRGE | ---GGFGFTLRGD | ----- | SPVLIAAVVPGQAEsAG | ---535 | |
| gi 7499828 | 46 | RPHVVKVKSE | ---TGFGENVKQVSEgql | rlsngql | yaPLQHVSAVLRRAADQAG | ---100 | |
| gi 8247939 | 410 | IHVTILHKEEG | ---AGLGFSLAGGADLEn | ----- | KVITVHRVFPNGLASQEGt | ---454 | |
| | | 70 | 80 | 90 | 100 | | |
| | |*.....*.....*.....*..... | | | | | |
| consensus | 45 | -LKPGDVILEVNG | -TSVEGLTHLEAVDLKE | -AGG | ---KVTLTVLRGG | 86 | |
| GRBP2 | 552 | -AREGDYIVS | IQL-VDC | KWLTISEVMKLIKsfGED | -----EIEKKVvall | 594 | |
| gi 13096475 | 117 | -ARAGDVITVDG | -TAVKGLSLYDVSLD | LQG-EADs | ---QVEVVLHAPG | 159 | |
| gi 7512038 | 445 | -LMPGDKILKVD | -MDMNGVTREEA | VLFLLS-LQD | ---RIDLVQYCK | 486 | |
| gi 6671754 | 532 | -LKVGDRIVS | ING-QPIDGLSH | TDVAVNLKN-AFG | ---RIILQVADT | 573 | |
| gi 7662086 | 83 | -VKEGDRIIKVNG | tMYTNSS-HLEV | VKLKISg | -----aYVALTILGSS | 123 | |
| gi 131530 | 552 | kINEGDQIVLINGr | -DISEHTHDQVVMF | IKa-SREshsrELALVIRRA | 598 | | |
| gi 6093970 | 536 | -LKEGDYIVSVNG | -QPCKWKHLEWVTQLRS | -MGE | ---GVSILQVWSLL | 578 | |
| gi 7499828 | 101 | -LRKGDRIILEVNG | -LNVES | THRKVDLINK-GGD | ---ELTMIVISVE | 142 | |
| gi 8247939 | 455 | -IQKNEVLS | ING-KSLKGTTHD | ALAILRQ-AREp | ---RQAVIVTRKl | 497 | |

FIG. 2
Genomic structure of human GRBP2

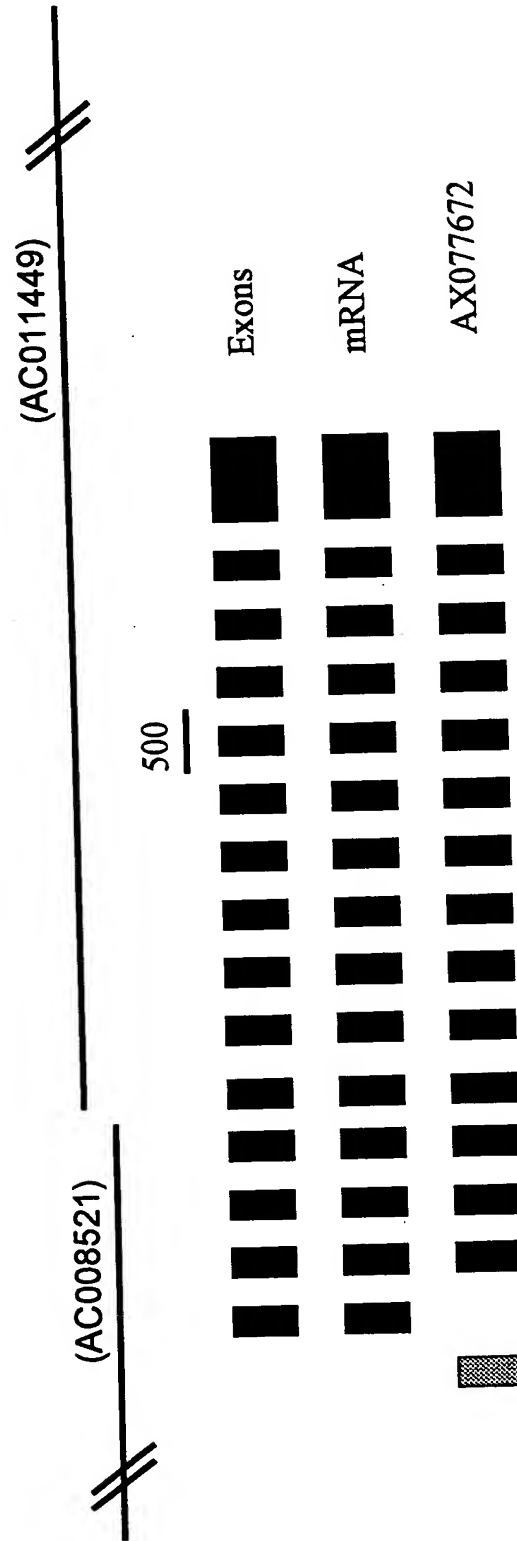


Fig. 3

Nucleotide and protein sequence of the GRBP2 gene

nt: SEQ ID NO: 1

aa: SEQ ID NO: 3

| | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| | | | | | | | M | T | D | A | L | L | 6 |
| tc | cgc | gcc | cgc | gcc | gct | agc | ATG | ACC | GAC | GCG | CTG | TTG | 38 |
| P | A | A | P | Q | P | L | E | K | E | N | D | G | 19 |
| CCC | GCG | GCC | CCC | CAG | CCG | CTG | GAG | AAG | GAG | AAC | GAC | GGC | 77 |
| Y | F | R | K | G | C | N | P | L | A | Q | T | G | 32 |
| TAC | TTT | CGG | AAG | GGC | TGT | AAT | CCC | CTT | GCA | CAA | ACC | GGC | 116 |
| R | S | K | L | Q | N | Q | R | A | A | L | N | Q | 45 |
| CGG | AGT | AAA | TTG | CAG | AAT | CAA | AGA | GCT | GCT | TTG | AAT | CAG | 155 |
| Q | I | L | K | A | V | R | M | R | I | G | A | E | 58 |
| CAG | ATC | CTG | AAA | GCC | GTG | CGG | ATG | AGG | ATC | GGA | GCG | GAA | 194 |
| N | L | L | K | V | A | T | N | S | K | V | R | E | 71 |
| AAC | CTT | CTG | AAA | GTG | GCC | ACA | AAC | TCA | AAG | GTG | CGG | GAG | 233 |
| Q | V | R | L | E | L | S | F | V | N | S | D | L | 84 |
| CAA | GTG | CGG | CTG | GAG | CTG | AGC | TTC | GTC | AAC | TCA | GAC | CTG | 272 |
| Q | M | L | K | E | E | L | E | G | L | N | I | S | 97 |
| CAG | ATG | CTC | AAG | GAA | GAG | CTG | GAG | GGG | CTG | AAC | ATC | TCG | 311 |
| V | G | V | Y | Q | N | T | E | E | A | F | T | I | 110 |
| GTG | GGC | GTC | TAT | CAG | AAC | ACA | GAG | GAG | GCA | TTT | ACG | ATT | 350 |
| P | L | I | P | L | G | L | K | E | T | K | D | V | 124 |
| CCC | CTG | ATT | CCT | CTT | GGC | CTG | AAG | GAA | ACG | AAA | GAC | GTC | 389 |
| D | F | A | V | V | L | K | D | F | I | L | E | H | 137 |
| GAC | TTT | GCA | GTC | GTC | CTC | AAG | GAT | TTT | ATC | CTG | GAA | CAT | 428 |
| Y | S | E | D | G | Y | L | Y | E | D | E | I | A | 150 |
| TAC | AGT | GAA | GAT | GGC | TAT | TTA | TAT | GAA | GAT | GAA | ATT | GCA | 467 |
| D | L | M | D | L | R | Q | A | C | R | T | P | S | 163 |
| GAT | CTT | ATG | GAT | CTG | AGA | CAA | GCT | TGT | CGG | ACG | CCT | AGC | 506 |

| | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
| R | D | E | A | G | V | E | L | L | M | T | Y | F | 176 |
| CGG | GAT | GAG | GCC | GGG | GTG | GAA | CTG | CTG | ATG | ACA | TAC | TTC | 545 |
| | | | | | | | | | | | | | |
| I | Q | L | G | F | V | E | S | R | F | F | P | P | 189 |
| ATC | CAG | CTG | GGC | TTT | GTC | GAG | AGT | CGA | TTC | TTC | CCG | CCC | 584 |
| | | | | | | | | | | | | | |
| T | R | Q | M | G | L | L | F | T | W | Y | D | S | 201 |
| ACA | CGG | CAG | ATG | GGA | CTC | CTG | TTC | ACC | TGG | TAT | GAC | TCT | 623 |
| | | | | | | | | | | | | | |
| L | T | G | V | P | V | S | Q | Q | N | L | L | L | 214 |
| CTC | ACC | GGG | GTT | CCG | GTC | AGC | CAG | CAG | AAC | CTG | CTG | CTG | 662 |
| | | | | | | | | | | | | | |
| E | K | A | S | V | L | F | N | T | G | A | L | Y | 227 |
| GAG | AAG | GCC | AGT | GTC | CTG | TTC | AAC | ACT | GGG | GCC | CTC | TAC | 701 |
| | | | | | | | | | | | | | |
| T | Q | I | G | T | R | C | D | R | Q | T | Q | A | 240 |
| ACC | CAG | ATT | GGG | ACC | CGG | TGC | GAT | CGG | CAG | ACG | CAG | GCT | 740 |
| | | | | | | | | | | | | | |
| G | L | E | S | A | I | D | A | F | Q | R | A | A | 253 |
| GGG | CTG | GAG | AGT | GCC | ATA | GAT | GCC | TTT | CAG | AGA | GCC | GCA | 779 |
| | | | | | | | | | | | | | |
| G | V | L | N | Y | L | K | D | T | F | T | H | T | 266 |
| GGG | GTT | TTA | AAT | TAC | CTG | AAA | GAC | ACA | TTT | ACC | CAT | ACT | 818 |
| | | | | | | | | | | | | | |
| P | S | Y | D | M | S | P | A | M | L | S | V | L | 279 |
| CCA | AGT | TAC | GAC | ATG | AGC | CCT | GCC | ATG | CTC | AGC | GTG | CTC | 857 |
| | | | | | | | | | | | | | |
| V | K | M | M | L | A | Q | A | Q | E | S | V | F | 292 |
| GTC | AAA | ATG | ATG | CTT | GCA | CAA | GCC | CAA | GAA | AGC | GTG | TTT | 896 |
| | | | | | | | | | | | | | |
| E | K | I | S | L | P | G | I | R | N | E | F | F | 305 |
| GAG | AAA | ATC | AGC | CTT | CCT | GGG | ATC | CGG | AAT | GAA | TTC | TTC | 935 |
| | | | | | | | | | | | | | |
| M | L | V | K | V | A | Q | E | A | A | K | V | G | 318 |
| ATG | CTG | GTG | AAG | GTG | GCT | CAG | GAG | GCT | GCT | AAG | GTG | GGA | 974 |
| | | | | | | | | | | | | | |
| E | V | Y | Q | Q | L | H | A | A | M | S | Q | A | 331 |
| GAG | GTC | TAC | CAA | CAG | CTA | CAC | GCA | GCC | ATG | AGC | CAG | GCG | 1013 |
| | | | | | | | | | | | | | |
| P | V | K | E | N | I | P | Y | S | W | A | S | L | 344 |
| CCG | GTG | AAA | GAG | AAC | ATC | CCC | TAC | TCC | TGG | GCC | AGC | TTA | 1052 |
| | | | | | | | | | | | | | |
| A | C | V | K | A | H | H | Y | A | A | L | A | H | 357 |
| GCC | TGC | GTG | AAG | GCC | CAC | CAC | TAC | GCG | GCC | CTG | GCC | CAC | 1091 |
| | | | | | | | | | | | | | |
| Y | F | T | A | I | L | L | I | D | H | Q | V | K | 370 |
| TAC | TTC | ACT | GCC | ATC | CTC | CTC | ATC | GAC | CAC | CAG | GTG | AAG | 1130 |

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|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
| P | G | T | D | L | D | H | Q | E | K | C | L | S | 383 |
| CCA | GGC | ACG | GAT | CTG | GAC | CAC | CAG | GAG | AAG | TGC | CTG | TCC | 1169 |
| Q | L | Y | D | H | M | P | E | G | L | T | P | L | 396 |
| CAG | CTC | TAC | GAC | CAC | ATG | CCA | GAG | GGG | CTG | ACA | CCC | TTG | 1208 |
| A | T | L | K | N | D | Q | Q | R | R | Q | L | G | 409 |
| GCC | ACA | CTG | AAG | AAT | GAT | CAG | CAG | CGC | CGA | CAG | CTG | GGG | 1247 |
| K | S | H | L | R | R | A | M | A | H | H | E | E | 422 |
| AAG | TCC | CAC | TTG | CGC | AGA | GCC | ATG | GCT | CAT | CAC | GAG | GAG | 1286 |
| S | V | R | E | A | S | L | C | K | K | L | R | S | 435 |
| TCG | GTG | CGG | GAG | GCA | AGC | CTC | TGC | AAG | AAG | CTG | CGG | AGC | 1325 |
| I | E | V | L | Q | K | V | L | C | A | A | Q | E | 448 |
| ATT | GAG | GTG | CTA | CAG | AAG | GTG | CTG | TGT | GCC | GCA | CAG | GAA | 1364 |
| R | S | R | L | T | Y | A | Q | H | Q | E | E | D | 461 |
| CGC | TCC | CGG | CTC | ACG | TAC | GCC | CAG | CAC | CAG | GAG | GAG | GAT | 1403 |
| D | L | L | N | L | I | D | A | P | S | V | V | A | 474 |
| GAC | CTG | CTG | AAC | CTG | ATC | GAC | GCC | CCC | AGT | GTT | GTT | GCT | 1442 |
| K | T | E | Q | E | V | D | I | I | L | P | Q | F | 487 |
| AAA | ACT | GAG | CAA | GAG | GTT | GAC | ATT | ATA | TTG | CCC | CAG | TTC | 1481 |
| S | K | L | T | V | T | D | F | F | Q | K | L | G | 500 |
| TCC | AAG | CTG | ACA | GTC | ACG | GAC | TTC | TTC | CAG | AAG | CTG | GGC | 1520 |
| P | L | S | V | F | S | A | N | K | R | W | T | P | 513 |
| CCC | TTA | TCT | GTG | TTT | TCG | GCT | AAC | AAG | CGG | TGG | ACG | CCT | 1559 |
| P | R | S | I | R | F | T | A | E | E | G | D | L | 526 |
| CCT | CGA | AGC | ATC | CGC | TTC | ACT | GCA | GAA | GAA | GGG | GAC | TTG | 1598 |
| G | F | T | L | R | G | N | A | P | V | Q | V | H | 539 |
| GGG | TTC | ACC | TTG | AGA | GGG | AAC | GCC | CCC | GTT | CAG | GTT | CAC | 1637 |
| F | L | D | P | Y | C | S | A | S | V | A | G | A | 552 |
| TTC | CTG | GAT | CCT | TAC | TGC | TCT | GCC | TCG | GTG | GCA | GGA | GCC | 1676 |
| R | E | G | D | Y | I | V | S | I | Q | L | V | D | 565 |
| CGG | GAA | GGA | GAT | TAT | ATT | GTC | TCC | ATT | CAG | CTT | GTG | GAT | 1715 |
| C | K | W | L | T | L | S | E | V | M | K | L | L | 578 |
| TGT | AAG | TGG | CTG | ACG | CTG | AGT | GAG | GTT | ATG | AAG | CTG | CTG | 1754 |

| | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
| K | S | F | G | E | D | E | I | E | M | K | V | V | 591 |
| AAG | AGC | TTT | GGC | GAG | GAC | GAG | ATC | GAG | ATG | AAA | GTC | GTG | 1793 |
| S | L | L | D | S | T | S | S | M | H | N | K | S | 604 |
| AGC | CTC | CTG | GAC | TCC | ACA | TCA | TCC | ATG | CAT | AAT | AAG | AGT | 1832 |
| A | T | Y | S | V | G | M | Q | K | T | Y | S | M | 617 |
| GCC | ACA | TAC | TCC | GTG | GGA | ATG | CAG | AAA | ACG | TAC | TCC | ATG | 1871 |
| I | C | L | A | I | D | D | D | D | K | T | D | K | 630 |
| ATC | TGC | TTA | GCC | ATT | GAT | GAT | GAC | GAC | AAA | ACT | GAT | AAA | 1910 |
| T | K | K | I | S | K | K | L | S | F | L | S | W | 643 |
| ACC | AAG | AAA | ATC | TCC | AAG | AAG | CTT | TCC | TTC | CTG | AGT | TGG | 1949 |
| G | T | N | K | N | R | Q | K | S | A | S | T | L | 656 |
| GGC | ACC | AAC | AAG | AAC | AGA | CAG | AAG | TCA | GCC | AGC | ACC | TTG | 1988 |
| C | L | P | S | V | G | A | A | R | P | Q | V | K | 669 |
| TGC | CTC | CCA | TCG | GTC | GGG | GCT | GCA | CGG | CCT | CAG | GTC | AAG | 2027 |
| K | K | L | P | S | P | F | S | L | L | N | S | D | 682 |
| AAG | AAG | CTG | CCC | TCC | cct | ttc | agc | ctt | ctc | aac | tca | gac | 2066 |
| S | S | W | Y | * | | | | | | | | | 686 |
| agt | tct | tgg | tac | taa | tgt | gag | gaa | aca | aac | atg | ttc | agg | 2105 |
| ccc | cga | aca | ttt | ccg | gtg | ctg | act | cgg | cct | taa | acg | ttt | 2144 |
| gtg | cca | taa | tgg | aaa | ata | tct | atc | tat | ctg | ttg | tca | aat | 2183 |
| cct | gtt | ttt | ctc | ata | gtg | taa | act | cac | att | tga | tgt | gtt | 2222 |
| ttt | atg | aag | gaa | agt | aac | caa | gaa | acc | tct | agg | aat | tag | 2261 |
| tga | aaa | aag | aac | ttt | ttt | gag | gtg | tgt | tac | tat | act | gct | 2300 |
| gta | agt | tat | tta | tta | tat | aaa | gta | ttg | taa | ata | gaa | tag | 2339 |
| tgt | tga | aga | tat | gaa | ata | tgg | cta | ctt | tta | atg | gtg | aca | 2378 |
| att | atg | act | ttt | agt | cac | tat | taa | att | ggg | gtt | acc | tat | 2417 |
| atc | agt | aca | att | tgt | agt | tgt | ttc | cag | gtt | tgg | cta | ata | 2456 |
| atc | att | cct | taa | cct | aga | att | cag | atg | atc | ctg | gaa | tta | 2495 |
| agg | cag | gtc | aga | gga | ctg | taa | tga | tag | aat | taa | att | agt | 2534 |
| gtc | act | aaa | aac | tgt | ccc | aaa | gtg | ctg | ctt | cct | aat | agg | 2573 |

| | |
|---|------|
| aat tca tta acc taa aac aag atg tta cta tta tat cga | 2612 |
| tag act atg aat gct att tct aga aaa agt cta gtg cca | 2651 |
| aat ttg tct tat taa ata aaa aca atg tag gag cag ctt | 2690 |
| ttc ttc tag ttt gat gtc att taa gaa tta cta aca cag | 2729 |
| tgg cag tgt tag atg aag atg ctg tct aca agg tag ata | 2768 |
| ata tac tgt ttg ata ctc aaa aca ttt ttc att ttg ttt | 2807 |
| aaa gta gaa gtt aca taa ttc tat att tta agt ctt ggg | 2846 |
| taa aaa agt agt ttt aca ttt tat aaa gta aag atg taa | 2885 |
| atg att cag gtt taa agc tct att tga ctt cct ttt ttt | 2924 |
| gtt tga gat agc gtc ttg ctg tgt tgc cca ggc tgg agt | 2963 |
| gca gtg gtg tga tct cag ctc agt gca acc tcc gcc ccc | 3002 |
| tgg gat caa gcg att ctc cta cct cag cct ccc aaa tag | 3041 |
| ctg gga cta caa ggt gcc ctc cag cat gcc tgg ctg att | 3080 |
| ttt gta ttt tta gtt gag gtg agg ttt cac cat gtt ggc | 3119 |
| cag gcg ggt ttc gaa atc ctg acc tca aat gat cca ccc | 3158 |
| acc tca gcc tcc caa agt gct ggg att aca ggc atg agc | 3197 |
| cac cac aac cgt ccc act att tta ctt ttt aaa atg aca | 3236 |
| ttc cta ctg att gat ttt tat ctt gct ata agt tcg atg | 3275 |
| aca ccg tga atc taa taa ggt tca ctg ttg aca cag tac | 3314 |
| aag tta cat agc taa aat aca tag cat tga aga cta att | 3353 |
| tta agg att gac aag agt tta ttt tct att gtg caa tat | 3392 |
| ctt aaa gga agc aac cac ctt tgg gaa agt gta tct gct | 3431 |
| gct cct agg gcc atg ctt gta tac ata ttt aaa taa aca | 3470 |
| tat tca ttt acc cg | 3484 |